

**REMARKS**

**Status of the Claims**

Claims 1-38 are pending in this application. Claims 39-40 have been added.

Claim 39, as compared to claim 18, additionally recites that the treatment of primary and secondary tumors is “by modulating the proliferation of tumors”. Support for this language can be found at page 4, line 27 of the Specification (with reference to the published PCT text).

Claim 40 additionally recites that the treatment of primary and secondary tumors by inhibiting angiogenesis with respect to angiogenesis “associated with tumor proliferation”. This language is support by the Specification at, for example, page 1, line 5 of the Specification.

**1. Claim Rejections - 35 U.S.C. § 103**

Applicants note with appreciation that the previous rejection of the claims for obviousness over Willoughby et al. in view of Pressato et al. has been removed. But claims 18, 22-27, 30 and 36 have now been rejected under 35 U.S.C. § 103(a) over Berkeley et al. in view of Pressato et al. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants fundamentally submit that the Examiner’s new combination of references is no more relevant than the previous combination of references, so that this new prior art rejection should be removed for the same reasons as previously discussed.

The present claims are limited to use of a 100% benzyl esterified hyaluronic acid (also known as a total benzyl ester) for the treatment and care of primary and secondary tumors by applying at the tumor site a biomaterial comprised of the total benzyl ester. Neither of the references cited by the Examiner teach or suggest this method of treatment utilizing the total benzyl ester of hyaluronic acid, and previously submitted Declaration evidence establishes the unexpectedly improved results achieved by the present invention as compared to the closest prior art, thereby

rebutting any *prime facie* case of obviousness. As noted by the Examiner, Berkeley et al. merely disclose that myomectomy itself may decrease fertility in women, probably on the basis of adhesion formation. The reference does not at all teach or suggest benzyl esters of hyaluronic acid, or the total benzyl ester of hyaluronic acid, for the treatment and care of primary and secondary tumors.

Applicants submit that Berkeley et al. is actually farther removed from the present invention than the Examiner's previous primary reference to Willoughby et al. Therefore, Applicants submit that it is improper for the Examiner to drop a rejection which has been overcome by comparative test results and institute a new prior art rejection with prior art that is actually worse or further removed than the previously cited prior art.

But even considering the Examiner's combination of references, this combination first of all does not even establish a *prime facie* case of obviousness. For there to be a proper *prime facie* case of obviousness, there must be some motivation to combine the references as suggested by the Examiner. The Examiner's secondary reference, Pressato et al., teaches nothing concerning inhibition of angiogenesis or of tumor growth, nor anything regarding granulation tissue. Thus, there would be no motivation for those skilled in the art to utilize the materials of Pressato et al. for the method of the present invention, nor to utilize the materials of Pressato et al. for the methods described by Berkeley et al.

But even assuming *arguendo* that the Examiner has established a case of *prime facie* obviousness, that position is rebutted by experimental evidence that is already of record. As noted above, Pressato et al. does not suggest the use of a total benzyl ester of hyaluronic acid for inhibiting angiogenesis. At most Pressato et al. discloses different types of benzyl ester products, that is, a partially esterified product and a total esterified product with two types of alcohols to produce a mixed ester (see Pressato et al., page 9, lines 8-25, Examples 3 and 4). Test results in the present application, however, show that while the presently claimed total benzyl ester of hyaluronic acid inhibits angiogenesis as required in the method of the present

invention, some forms of hyaluronic acid, including partial benzyl esters of hyaluronic acid, actually stimulate angiogenesis. Clearly this is critically opposite to the purpose and treatment of the present invention. Thus, one skilled in the art would not at all be motivated to combine Pressato et al. with Berkeley et al. and one skilled in the art would clearly have no reasonable expectation of success in achieving the claimed invention based on the two references cited by the Examiner.

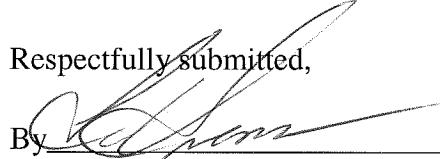
In view of the above, reconsideration and withdrawal of the rejections are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By 

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